done during baseline, during isoproterenol infusion (0.15 μg/kg/min) and during acute LV failure by coronary microembolization. *Results:* Along the LV inflow tract there was an early diastolic positive gradient (PLVmitral-PLVapex) of 1.6 ± 1.1 mmHg (mean ± SD) towards the apex. Along the outflow tract there was an early-diastolic pressure gradient towards the subaortic region (PLVapex-PLVsubaorta) of 3.5 ± 1.0 mmHg. The pressure gradients and velocities increased with isoproterenol and decreased with failure (see table). The PLVmitral-PLVapex correlated with peak mitral-to-apical flow velocity ($r = 0.67$, $p < 0.05$), and the PLVapex-PLVsubaorta correlated with peak apex-subaorta flow velocities ($r = 0.82$, $p < 0.05$).

	Baseline	Failure	Isoproterenol
PLVmitral-PLVapex (mmHg)	1.6 ± 1.1#	1.0 ± 0.7#*	2.6 ± 2.1#*
PLVapex-PLVsubaorta (mmHg)	3.5 ± 1.0#	1.5 ± 1.0#*	3.9 ± 1.4#

#p < 0.05 when comparing local pressures: *p < 0.05 vs baseline.

Conclusion: This study shows the existence of different intraventricular diastolic pressure gradients in the LV inflow and outflow tract. The gradients and flow velocities were modified by changes in inotropy and ischemia.

930 Predictors and Markers of Heart Failure Outcome

Monday, March 17, 1997, Noon–2:00 p.m.
Anaheim Convention Center, Hall E
Presentation Hour: Noon–1:00 p.m.

930-155 Obesity in Hypertensive African-Americans Predicts Development of Left Ventricular Systolic Dysfunction

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Although epidemiologic data suggest that 50 million Americans have hypertension (HTN), systolic dysfunction secondary to HTN alone (HTNCM) rarely develops. Recent work suggests that race and body mass (BMI) are independent risk factors for congestive heart failure (CHF). We investigated the relationship between body mass, race and HTN in patients (pts) with symptomatic CHF (NYHA Class 2.8 ± 0.8, mean ± SD) in a prospective study of 557 pts with reduced LV ejection fraction (LVEF), mean LVEF 25% ± 13%. Primary etiology of HTNCM was assigned only after *exclusion* of other etiologies and meeting our criteria for HTN: a) current or previous antihypertensive pharmacologic therapy or b) documentation of systolic blood pressure (SBP) reading of ≥140 mmHg or diastolic (DBP) ≥90 mmHg on 3 separate occassions. We found African-Americans (AAs) more likely to have HTN as the primary cardiomyopathy etiology than Caucasians (Cc), 75% vs 25%, $p < 0.001$ but no racial difference was seen in pts having a history of HTN and another CHF primary etiology (2nd HTN), 48% vs 52%, p = NS. HTNCM pts were older at presentation than the other 2 groups combined, (54 ± 12 yrs. vs 50 ± 14 yrs., $p = 0.02$) and had higher baseline LVEF (28 ± 13% vs 24 + 12%, $p < 0.01$). As expected, HTNCM pts had higher resting SBP and DBP than 2nd HTN pts or in pts with no HTN (SBP: 135 ± 23 mmHg vs 121 ± 20 mmHg vs 111 ± 17 mmHg, $p < 0.01$; DBP: 87 ± 15 mmHg vs 78 ± 14 mmHg vs 72 ± 12 mmHg, $p < 0.01$). Although no difference was seen in height between the 3 groups, (172 ± 11 cm vs 172 ± 10 cm vs 173 ± 10 cm, p = NS) HTNCM pts were more obese than pts with 2nd HTN or pts with no HTN (89 ± 24 kg vs 79 ± 20 kg vs 75 ± 18 kg, $p < 0.01$) resulting in HTNCM pts having greater body mass index (kg/Ht^2) than 2nd HTN pts or pts with no HTN (30 ± 7 vs 27 ± 7 vs 25 ± 5, $p < 0.01$). Using multicategory logistic modeling to predict development of HTNCM in our population, the only interaction found was elevated body mass index in African American pts ($p < 0.01$).

Conclusion: Hypertensive cardiomyopathy with systolic dysfunction occurs more frequently in African Americans with elevated body mass index than in Caucasians with elevated body mass index or in non-obese patients of either race.

930-156 Gender and Quality of Life in African Americans With Congestive Heart Failure

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Quality of life is important in the evaluation of congestive heart failure. To analyze quality of life in African Americans (AA), the Medical Outcomes Study (SF-36) and the Minnesota Living with Heart Failure (LIhFE) questionnaires were administered to 114 AA patients with congestive heart failure by NHANES criteria, (46 men, age 64 ± 17 yrs.; 68 women, age 68 ± 11 yrs.). Mean scores for the LIhFE were physical dimension 16, emotional dimension 5 total 31. All scores were comparable to norms for patients treated for CHF in earlier studies.

SF-36 Scales	Male	Female	Group	Norms
Physical functioning	50.91	33.64*	40.55	47.54
Role/physical	58.52	43.18**	49.32	34.37
Bodily Pain	74.05	61.15*	66.31	62.67
General Health	55.73	49.48	51.58	47.05
Vitality	52.05	42.5*	46.32	44.29
Social functioning	77.27	69.87	72.84	71.31
Role-Emotional	75.19	77.95	76.85	63.67
Mental Health	74.82	70.15	72.04	74.68

*p < 0.05 male vs female: **p = 0.06

Stepwise linear regression analysis identified 3 of 16 variables, angina, income and treatment with one of three CHF drugs, as predictors of quality of life. These data suggest that in AA with CHF, men have higher self-assessment of their physical function and vitality than women, but assessment of social functioning, emotional, mental and general health is similar in men and women. In AA with CHF, physical and emotional role function is maintained at a higher level than in other groups with CHF, but overall quality of life is not significantly lower.

930-157 Cachexia as Independent Predictor of Survival in Heart Failure

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Cardiac cachexia is long recognised, but little investigated. We sought to determine, whether the cachectic state in chronic heart failure (CHF) provides additional prognostic information for all-cause mortality. Between June 1993 and May 1995 we assessed in 167 consecutive CHF patients (16 female) treadmill exercise capacity (peak VO_2 17.5 ± 6.8 ml/kg/min, mean ± SD) and functional status (NYHA I: n = 21, II: 59, III: 68, IV: 19, LVEF 30 ± 15% (n = 114), age 61 ± 10 y). Cachexia was prospectively defined on the basis of a non-intentional documented weight loss of > 7.5% of previous normal weight (n = 28, range 9–36%, i.e. 6–30 kg) in ≥6 months.

Results: Censoring the follow-up in June 1996, 38 patients had died after a mean of 238 ± 221 d (follow-up of survivors 676 ± 197 d). The cachectic state was predictive of survival independently of age, NYHA class, LVEF and peak VO_2. The mortality in the cachectic cohort was 18% at 3 months (mo), 32% at 6 mo, 39% at 12 mo, and 50% at 18 mo. Patients with a peak VO_2 < 14 ml/kg/min (respective mortality 17, 28, 38, and 43%) *and* defined as cachectic had a 1-year survival of 38% (18 mo: 23%), compared to 96% (18 mo: 91%), in patients with neither of these two risk factors (both $p < 0.0001$).

Conclusion: The cachectic state is an independent risk factor of survival in CHF. Combined with a low peak VO_2 it identifies an extremely high-risk subset of CHF patients. Its assessment should be included in transplant assessment programmes and intervention studies that aim at survival analyses.

930-158 Immunocytokine Modulation Predicts Adverse Clinical Outcome In Advanced Heart Failure

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Immunocytokine (IC) activation has been implicated in the progression of chronic heart failure (HF). The soluble form of ICAM-1 (sICAM-1) is elevated in HF and correlates with disease severity. The prognostic value of modulation of circulating sICAM-1 in concert with neurohormonal factors, during recovery from decompensated heart failure has not been hitherto investigated. We studied 14 HF patients (NYHA IV; EF < 0.2) with decompensated HF due to low cardiac output (CO) state. Invasive hemodynamic monitoring, including CO, mean pulmonary artery pressure (mPA), and pulmonary vascular resistance (PVR), were measured before and after 72 hours of intravenous milrinone (0.5 μg/kg/min). Soluble ICAM-1, brain natriuretic peptide (BNP), and pulmonary endothelin (Etp) levels were measured at baseline and end of therapy. Patients were evaluated at study end and Day 7 of therapy by the six-minute walk test. *Results:* Nine patients demonstrated improvement in functional class [NYHA 2.7, Group 1], while 5 patients failed to improve [NYHA 4, Group 2]. Comparisons of hemodynamics, immunocytokine and neurohormonal changes in the two groups are shown in the table.

Only increase in sICAM-1 and persistant Etp release at the end of therapy

	Group 1		p	Group 2		p
CI (L/min/m^2)	1.7 ± 0.3	2.9 ± 0.3	< 0.01	1.8 ± 0.4	3 ± 0.4	< 0.01
MPA mmHg	47 ± 4	32 ± 5	< 0.01	52 ± 3	30 ± 3	< 0.01
PVRdynecm	358± 34	206± 24	< 0.01	419± 24	209 ± 21	< 0.01
sICAM ng/ml	420± 98	350± 86	< 001	502± 98	532 ± 95	< 0.05*
BNP pg/ml	202± 39	104± 34	< 0.001	340± 78	180 ± 39	< 0.01
Etp pg/min	18 ± 8	0.6 ± 6	< 0.001	23 ± 4	13 ± 8	< 0.05*

*Group 1 vs Group 2 variables at termination (p < 0.01)

in group 2 were adverse outcome predictors, despite similar hemodynamic improvement. *Inferences:* 1). Soluble ICAM-1 levels decrease in parallel with BNP and ETp during recovery from decompensated HF. 2) Lack of reduction in sICAM-1 levels, along with persistant Etp are more powerful adverse prognostic indicators than hemodynamic response.

930-159 Free Radical Activity Increases with NYHA Class in Congestive Heart Failure

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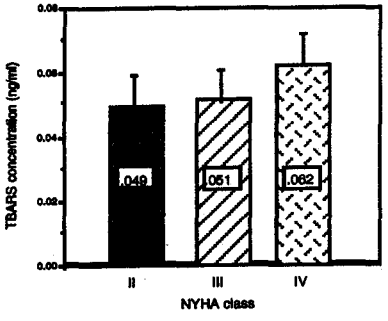
Oxygen free radicals have been implicated in the genesis and progression of congestive heart failure (CHF). It has been demonstrated that thiobarbituric acid reactive substances (TBARS), which are markers of lipid peroxidation, are elevated in CHF patients compared to controls.

In this study, we correlated TBARS with NYHA functional class. TBARS were measured by spectrophotometry in the plasma of 54 patients with CHF. The mean age of the patients was 61 yrs (range: 29–87) and the mean baseline ejection fraction was 19% (range: 5–38). Ten patients were NYHA class II, 32 were class III, and 12 were class IV. There were 46 males and 8 females, of whom 21 had an ischemic etiology, 28 had idiopathic CHF and 4 had prior valvular heart disease.

As shown in the graph (mean TBARS conc. ± S.D.), there was a progressive increase in TBARS with NYHA class; p = 0.0211 by ANOVA. Thus, patients with CHF have increased oxygen free radical production and/or decreased reducing ability.



TBARS directly correlate with worsening functional class. This may have therapeutic and prognostic implications in CHF.

930-160 Serum Uric Acid is Related to Lower Limb Blood Flow in Patients with Chronic Heart Failure

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In chronic heart failure (CHF), there is limitation of blood flow to the legs during exercise. Elevations in serum uric acid levels occur in situations which involve an impairment of vascular function, and following interruption of blood flow to skeletal muscle. We sought to determine whether serum uric acid is related to lower limb blood flow in patients with CHF. To this end, lower limb blood flow was measured at rest (RBF) and at the peak of exercise (PBF) in 22 patients with CHF using strain-gauge venous occlusion plethysmography. All patients underwent a metabolic assessment, which included an intravenous glucose tolerance test (IVGTT) (to obtain an index of insulin sensitivity) and measurement of serum uric acid. Mean (± SEM) RBF and PBF were 2.87 (0.23) and 24.00 (1.83) ml/100 ml/min, respectively. Patients in the upper tertile of serum uric acid concentrations had significantly lower PBF than those in the lowest tertile [15.9 (2.2) v 31.0 (2.1) ml/100 ml/min (mean (± SEM) p = 0.003]. Serum uric acid correlated with PBF (r = −0.86, p < 0.001), but not with RBF. In stepwise linear regression analysis, uric acid emerged as the only predictor of peak blood flow [SC = −0.83 (p < 0.001), R^2 = 0.73, (p < 0.001)], *independently of* diuretic dose, age, body mass index, plasma creatinine, fasting and IVGTT glucose and insulin, insulin sensitivity and alcohol intake. *Conclusion:* There is a strong inverse relationship between serum uric acid concentrations and PBF in the legs of patients with CHF. Further studies are needed to determine whether this association is linked to the known effects of xanthine oxidase-derived free radical release on vascular function.

930-173 Clinical Significance of Elevated Levels of Cardiac Troponin T Detected by Second Generation Assay in Patients with Congestive Heart Failure

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Recent study reported that a regulatory protein in the myocardium, cardiac troponin I level was elevated in circulating blood in end-stage congestive heart failure (CHF). However, there have been few reports for biochemical detection of myocardial damage in CHF. In the present study, to test the hypothesis that serum levels of cardiac troponin T (TnT) would be elevated in severe CHF patients and TnT level would be correlated with the severity of CHF, we measured TnT by newly developed second generation enzyme-linked immunosorbent assay using monoclonal antibodies 11-7 and M7 (detection limit 0.02 ng/ml vs 0.1 ng/ml in first generation assay, Boehringer Mannheim) in 31 patients with CHF and 169 healthy controls. TnT was detected in 17 of 31 patients with CHF (54.8%), but only 7 of 169 controls (4.1%, p < 0.001). All NYHA class IV (9/9) and 8 of 12 NYHA class III (66.7%) patients showed TnT ≥ 0.02 ng/ml, but TnT was not detected in NYHA class II patients (0/10). In patients with detected TnT, CTR (%) and plasma atrial natriuretic peptide (ANP) concentration (ng/ml) at hospitalization were significantly higher (p < 0.0005, p < 0.02).

	n	Age	CTR	ANP	CK (IU/l)	CK-MB (IU/l)
TnT ≥ 0.02 ng/ml	17	73 ± 13	69 ± 6	165 ± 78	113 ± 82	12 ± 12
TnT < 0.02 ng/ml	14	62 ± 13	59 ± 7	75 ± 86	120 ± 113	7 ± 4

In all 9 patients in whom TnT was elevated at hospitalization, TnT declined significantly after medical treatment. This study demonstrates the first evidence for elevated levels of TnT in severe CHF patients and suggests that latent myocardial damage generates in severe CHF patients.

930-174 The Relative Lymphocyte Concentration: A New Prognostic Marker in End-stage Heart Failure

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The physiologic stress suffered by ill patients results in an increased production of cortisol, and a shift in the leukocyte differential toward a decrease in the percentage of lymphocytes (% L). Automated analysis sampling thousands of cells has greatly reduced the assay variation in % L compared to manual methods. The purpose of this study was to examine the potential prognostic significance of a decrease in % L in patients with advanced heart failure. We identified 211 patients referred for consideration of heart transplantation, between April 1988 and July 1995, who did not have recent trauma, infection, myocardial infarction, corticosteroid use, or a history of malignancy. Over a mean follow-up of 84 months, there were 46 deaths (1-year survival 86%; 5-year survival 52%) and 90 transplants (1-year survival free from transplant of 58%; 5-year, 24%). Cox proportional hazards analysis showed a significant relationship between time to death and % L (p = 0.004), functional class (p = 0.002), and maximal oxygen uptake (p = 0.051). Kaplan-Meier survival of patients with an abnormal % L (<20.3%) was 78% at one year as compared to 90% in those with a normal % L. On multivariate analysis, both functional class (p < 0.0004) and % L (p < 0.004) are independent predictors of both survival and survival free from transplant. The % L is an inexpensive, readily available, and simple prognostic marker in patients with symptomatic heart failure. It should be incorporated into clinical models to predict subsequent patient outcome.

% L	Survival	
	1-year	5-year
<20.3%	78%	23%
> 20.3% (normal range)	90%	65%

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